REMARKS

Claims 16-18 and 21 are pending in the application. Claims 17, 18, and 21 are withdrawn from consideration. No amendments have been made by the present response.

Double Patenting

At pages 2-6 of the Office Action, claim 16 was finally rejected on the ground of nonstatutory obviousness-type double patenting over claim 1 of U.S. Patent No. 7,452,670 ("the '670 patent") in view of Duchen (2004) Diabetes 53:S96-S102.

Applicants respectfully traverse the rejection in view of the following remarks.

The inventors of the present application discovered that ruthenium red (a mitochondrial Ca++ porter) suppresses alpha synuclein-mediated toxicity in yeast expressing two copies of alpha synuclein (see Example 2 at page 32, lines 4-12 of the specification). This inventors' discovery that ruthenium red can be used to suppress alpha synuclein-mediated toxicity identifies ruthenium red as an agent that is expected to be effective in the treatment of Parkinson's disease.

Claim 16 is directed to a method of identifying a compound that inhibits alpha synuclein-mediated toxicity. Consistent with the inventors' experimental finding that ruthenium red can be used to suppress alpha synuclein-mediated toxicity, claim 16 contains steps including: contacting a yeast cell expressing alpha synuclein with a candidate agent such as a mitochondrial Ca++ porter (the elected species); and determining whether the candidate agent enhances viability of the cell.

Claim 1 of the '670 patent is directed to a method of identifying an agent that diminishes toxicity associated with alpha synuclein in a yeast cell that does not express the endogenous wild type gene glo4 or gtt1. Claim 1 of the '670 patent does not describe using ruthenium red as a means to suppress alpha synuclein-mediated toxicity. Furthermore, claim 1 of the '670 patent provides no hint that ruthenium red can be used for this purpose. As a result, claim 16 of the present application is unmistakably not a mere obvious variation of claim 1 of the '670 patent.

Duchen does not add what is lacking in claim 1 of the '670 patent. Duchen contains no disclosure related to alpha synuclein or its ability to induce cellular toxicity. With respect to Parkinson's disease, the introduction section of Duchen (pages S96-S97) contains only a general

statement that mitochondrial dysfunction has been implicated in many diseases, including Parkinson's disease (S97, left column). In a separate section of Duchen entitled "Mitochondrial Bioenergetics and Cellular Calcium Signaling," Duchen states that ruthenium red blocks the activity of an electrogenic uniporter that carries calcium into the mitochondria and that calcium that is accumulated by mitochondria must be removed (S97, right column). The "Mitochondrial Bioenergetics and Cellular Calcium Signaling" section of Duchen describes aspects of mitochondrial biology but does not explain or address mitochondrial defects associated with Parkinson's disease.

The Office Action concluded that, in view of the teachings of claim 1 of the '670 patent and Duchen, "one of ordinary skill in the art would have had a reasonable expectation of success to determine whether ruthenium red is a candidate agent that enhances viability of a cell (i.e. inhibit alpha synuclein) by combining the teachings of US PAT '670 with that of Duchen." Applicants strongly contest the Office Action's assessment of the relevance of Duchen's teachings to the claimed invention. In particular, nothing in Duchen would have led the person of ordinary skill in the art to reasonably expect (i) that mitochondrial calcium would be relevant to Parkinson's disease, and/or (ii) that ruthenium red would be effective at suppressing alpha synuclein-mediated toxicity or treating Parkinson's disease.

In its introduction section, Duchen states only that "mitochondrial dysfunction has been implicated" Parkinson's disease. Duchen does not suggest that the "mitochondrial dysfunction" of Parkinson's disease involves calcium uptake or calcium signaling or might be treatable with ruthenium red. The Office Action lacks any explanation as to how the person of ordinary skill in the art reading Duchen would have concluded that Duchen's general introductory statement about mitochondrial dysfunction in Parkinson's disease relates to Duchen's later specific teachings about mitochondrial biology in the section entitled "Mitochondrial Bioenergetics and Cellular Calcium Signaling." There is no connection in Duchen between these two sections that would have led the person of ordinary skill in the art to reasonably expect that ruthenium red would have any affect in modulating the "mitochondrial dysfunction" of Parkinson's disease, much less that it would be effective in suppressing alpha synuclein-mediated toxicity. Duchen's statements about the role of calcium signaling in mitochondrial bioenergetics and the effect of ruthenium red in blocking the activity of a uniporter that carries calcium into the mitochondria

would not have led to such an expectation. In the absence of a basis to reasonably expect that ruthenium red would suppress alpha synuclein-mediated toxicity, the person of ordinary skill in the art would have had no rationale for using ruthenium red in the practice of the method of claim 16.

In view of the foregoing remarks, the combination of claim 1 of the '670 patent and Duchen does not render claim 16 unpatentable. Applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a)

At pages 6-11 of the Office Action, claim 16 was finally rejected under 35 U.S.C. § 103(a) as being unpatentable over the '670 patent in view of Duchen for the same reasons provided in the double patenting rejection above.

With respect to the '670 patent, the double patenting rejection is necessarily limited to an analysis of whether claim 16 of the present application is patentably distinct from claim 1 of the '670 patent. In contrast, the present obviousness rejection may rely upon the whole content of the '670 patent. Notwithstanding this difference, the '670 patent (like claim 1 of the '670 patent) lacks any disclosure that would have led the person of ordinary skill in the art to expect that ruthenium red can be used as a means to suppress alpha synuclein-mediated toxicity. The inability of Duchen to remedy this deficiency is reviewed in detail above. The '670 patent and Duchen therefore fail to render claim 16 obvious for the same reasons provided above in the response to the double patenting rejection.

In view of these remarks, the combination of the '670 patent and Duchen does not render claim 16 unpatentable. Applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 17481-0002US1.

Respectfully submitted,

Date: February 24, 2012

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